REMARKS

Claim amendments

Claims 49-51 and 61 have been amended to replace "binding" specificity with "epitopic" specificity. Support for the amendment can be found, for example, on page 8, lines 14-15 and page 14, line 16.

Interview Summary

Applicants would like to take this opportunity to thank Examiner Ungar for the allowance of claims 45-48 and 52-55, and for her helpful comments for amending Claims 49-51 and 61 to overcome the prior art rejection during the telephonic interview with Applicant's Attorney on July 18, 2007. Applicant's Attorney requested the telephonic interview with Examiner Ungar to discuss the rejection of Claims 49-51 and 61 as being anticipated by Lin *et al, Proc. Natl. Sci. Coun., ROC Part B: Life Sciences, 22:*129-134 (1998).

In order to more clearly define Applicant's claimed invention over the teachings of the Lin *et al.* reference, Examiner Ungar suggested replacing "binding" specificity with "epitopic" specificity in Claims 49-51 and 61. Examiner Ungar further indicated that such amendment would appear to put Claims 49-51 and 61 in condition for allowance.

Applicant has amended Claims 49-51 in accordance with Examiner Ungar's suggestion.

Rejection of Claims 49-51 and 61 under 35 U.S.C. §102(b)

Claims 49-51 and 61 are rejected under 35 U.S.C. §102(b) "as being anticipated by Lin et al, PNAS, ROC part B: Life Sciences, 1998, 22:129-134" (Office Action, page 2). The Examiner states that the term "binding specificity" in Claims 49-51 and 61 "is not defined in the specification as originally filed" and that "it appears that the binding specificity claimed is drawn to the ability of the antibody to detect analyte as opposed to nonanalyte, for example the ability to detect the ouabain portion rather than the carrier portion of a ouabain-carrier complex" (Office Action, page 3). The Examiner further states that Lin *et al.* "teach the production of monoclonal antibody specific for ouabain using a ouabain-BSA construct . . .", that the monoclonal antibody produced binds to the ouabain as well as to the ouabain component of the ouabain-carrier

complex as disclosed in Figure 1, Method II" and "exemplifies the binding of the antibody to endogenous ouabain which does not comprise the carrier BSA construct (Table 1)" (Office Action, page 3). The Examiner concludes that the Lin *et al.* "monoclonal antibody has the same binding specificity as all of the claimed antibodies in that it binds to ouabain and the ouabain component of a ouabain-carrier complex" (Office Action, pages 3-4).

In the specification as filed Applicant defines binding specificity. Specifically, Applicant teaches that, in one aspect, the invention relates to "a monoclonal antibody or antigen binding fragment thereof that possesses substantially the same binding specificity (epitopic specificity) as one or more of the monoclonal antibodies described herein (*e.g.*, 1-10, 5A12, 7-1 and 8E4)" (specification, page 8, lines 13-16).

In Fig. 1 Lin *et al.* provides a schematic of a monoclonal antibody-based enzyme immunoassay for ouabain in which a mouse anti-ouabain monoclonal antibody binds to a ouabain-BSA conjugate and a sample antigen (Lin *et al.*, Fig. 1, Method II). However, as noted in the previously filed amendments, Lin *et al.* injected Balb/C mice with a ouabain-BSA conjugate (Oua-BSA) and spleen cells from mice showing the "highest titer against ***ouabain-BSA***" were fused to myeloma cells to generate hybridomas that produce ouabain monoclonal antibody (Lin *et al.*, page 131, column 2, emphasis added). Monoclonal antibodies produced by the hybridomas were then screened using the same antigen i.e., "ouabain-BSA conjugate" (Lin *et al.*, page 131, column 2). Thus, Lin *et al.* employed a method which selected for a monoclonal antibody having epitopic specificity for the ouabain-BSA conjugate. Although Lin *et al.* provide the schematic of Method II in Fig. 1, Lin *et al.* provide no evidence demonstrating that their monoclonal antibody produced epitopic specificity for ouabain using, for example, a competition ELISA using increasing concentrations of free ouabain. Based on the method Lin *et al.* used to generate the monoclonal antibody, it is likely that the monoclonal antibody has epitopic specificity for the ouabain-BSA conjugate, but not for ouabain alone. Further evidence of this is provided in Applicant's disclosure. In the specification as filed, Applicant used a method similar to that of Lin *et al.*, except that Applicant screened for antibodies having binding specificity for the hapten using a carrier in the hapten-carrier conjugate (i.e., Oua-BGG) that was different than the carrier of the hapten-carrier conjugate (i.e., Oua-BSA) used to immunize the animal in an attempt to obtain a ouabain mAb. Applicant teaches that "[f]usion of the spleen cells of mice

immunized with Oua coupled to BSA, HSA or BGG with plasmacytomas, yielded a very large number of clones secreting mAbs specific for the Oua-protein carrier" (specification, page 25, lines 4-6).

Since Applicant had previously overcome this rejection based on these facts presented in previously filed amendments, Applicant's Attorney requested a telephonic interview with Examiner to discuss this rejection. As indicated above, Examiner Ungar agreed to participate in a telephonic interview which took place on July 18, 2007. During the interview, Examiner Ungar stated that amending the claims to replace "binding" specificity with "epitopic" specificity would appear to place the claims in condition for allowance. As amended, the claims are directed to a monoclonal antibody or antigen binding fragment thereof having the same epitopic specificity as a monoclonal antibody produced by a hybridoma deposited under A.T.T.C. Accession Number PTA-812, PTA-813, PTA-814 or PTA-815, in accordance with the Examiner's helpful suggestion.

Lin *et al.* do not teach the subject matter of Applicant's claimed invention, particularly as amended.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,
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Date: August 7, 2007